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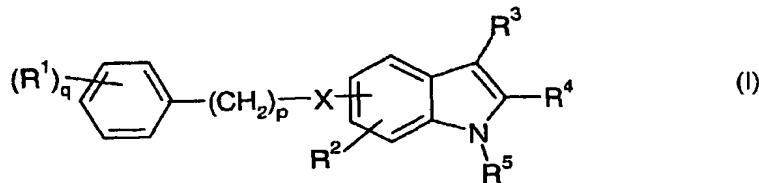
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For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.

(54) Title: INDOLE DERIVATIVES HAVING ANTI-ANGIOGENETIC ACTIVITY



(57) Abstract: The invention relates to the use of a compound of Formula (I), for the manufacture of a medicament to inhibit and/or reverse and/or alleviate symptoms of angiogenesis and/or any disease state associated with angiogenesis: Formula (I); wherein: X, p, q, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, and R<sup>5</sup> are as defined in the description. The invention also relates to use of compounds of Formula (I) as medica-  
ments and also to novel compounds of Formula (I). The invention further provides pharmaceutical compositions of compounds of Formula (I) and processes for the synthesis of compounds of Formula (I).

# INTERNATIONAL SEARCH REPORT

International Application No.

PCT/GB 03/01405

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/404 A61K31/405 C07D209/42 C07D209/18 C07D209/12  
A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K C07D A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BEILSTEIN Data, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 01 92224 A (ASTRAZENECA) 6 December 2001 (2001-12-06) cited in the application Abstract; page 1, lines 3-9; claims 1-13; examples.	1-12
A	US 4 533 672 A (FURR BARRINGTON J A ET AL) 6 August 1985 (1985-08-06) Abstract; claims 1-6.	1-12
P,X	WO 02 070478 A (ASTRAZENECA) 12 September 2002 (2002-09-12) Abstract; page 1, lines 2-8; claims 1-20; examples.	1-12
E	EP 1 297 833 A (PFIZER PROD INC) 2 April 2003 (2003-04-02) Abstract; claim 1.	1-12

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Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

### \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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- \*G\* document member of the same patent family

Date of the actual completion of the international search

22 December 2003

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# INTERNATIONAL SEARCH REPORT

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CH 414 639 A (SANDOZ AG) 15 June 1966 (1966-06-15) Claims; examples 2 and 3.	1-12
X	SHEPPARD G S: "3-(2-(3-Pyridinyl)thiazolidin-4-oyl)indoles, a novel series of platelet activating factor antagonists" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY, WASHINGTON, US, vol. 37, no. 13, 1994, pages 2011-2032, XP002170395 ISSN: 0022-2623	12
A	Page 2022, right column: preparation of 6-((4-fluorophenyl)methoxy)indole.	1-11
A	--- KWONG, F. Y.; BUCHWALD, S. L.: "A General, Efficient; and Inexpensive Catalyst System for the Coupling of Aryl Iodides and Thiols" ORG. LETT., vol. 4, no. 20, 2002, pages 3517-3520, XP002251752 Page 3519, table 2, entry 10.	1-12
A	--- DATABASE CROSSFIRE BEILSTEIN 'Online! Beilstein Institut zur Foerderung der chemischen Wissenschaften, Frankfurt/Main, DE; XP002251753 Database Accession No. 8172403 (BRN). & PHARM. CHEM. J. (ENGL. TRANSL.), vol. 32, no. 1, 1998, pages 29-32,	1-12
X	--- DATABASE CROSSFIRE BEILSTEIN 'Online! Beilstein Institut zur Foerderung der chemischen Wissenschaften, Frankfurt/Main, DE; XP002251754	12
A	Database Accession No. 183150 (BRN), Reaction 2 of 14.  & TETRAHEDRON, vol. 49, no. 48, 1993, pages 11155-11168, --- -/--	1-11

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/01405

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE CROSSFIRE BEILSTEIN 'Online! Beilstein Institut zur Foerderung der chemischen Wissenschaften, Frankfurt/Main, DE; XP002251755	12
A	Database Accession No. 207989 (BRN), Reaction 1 of 2.  & HELV. CHIM. ACTA, vol. 42, 1959, pages 2073-2098, ----	1-11
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A	Database Accession No. 5433848 (BRN), Reaction.  & CHEM. HETEROCYCL. COMPD. (ENGL. TRANSL.), vol. 27, no. 11, 1991, pages 1218-1221, ----	1-11
A	MONGE A ET AL: "NEW INDOLE AND PYRIDAZINOINDOLE ANALOGS - SYNTHESIS AND STUDY AS INHIBITORS OF PHOSPHODIESTERASES AND AS INHIBITORS OF BLOOD PLATELET AGGREGATION" ARCHIV DER PHARMAZIE, VCH VERLAGSGESELLSCHAFT MBH, WEINHEIM, DE, vol. 328, no. 10, October 1995 (1995-10), pages 689-698, XP000998422 ISSN: 0365-6233 Pages 690 and 695, compound 5. -----	1-12

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/GB 03/01405

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 1-12 (part)  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

As a result of the prior review under R. 40.2(e) PCT,  
no additional fees are to be refunded.

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☒ The additional search fees were accompanied by the applicant's protest.  
☐ No protest accompanied the payment of additional search fees.

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-12 (all part)

involving compounds (I), (V), (VIId), (VI), and (VIIdc)  
wherein R3 is different from cyano;

2. Claims: 1-12 (all part)

involving compounds (I), (V), (VIId), (VI), and (VIIdc)  
wherein R3 is cyano and R4 is different from amino and  
different from NR6R7.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-12 (part)

Second medical use claims 1-5 are in part functionally defined by reference to "disease states associated with angiogenesis", whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a limited number of such disease states (cf. page 1, lines 25-28). In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the claimed matter by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to angiogenesis and the disease states mentioned in the description, page 1, lines 25-28.

In addition, the scope of the claims 1-12 in as far as the expression prodrug is concerned, is so unclear (Article 6 PCT) that a meaningful search is impossible with regard to this expression. Consequently, the said claims have not been searched in as far as the term prodrug is concerned.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/01405

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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